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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/955,037	09/19/2001	Tom J. Whitaker	2959-0104P	8300

2292 7590 12/04/2002

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EXAMINER
LU, FRANK WEI MIN

ART UNIT	PAPER NUMBER
1634	12

DATE MAILED: 12/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/955,037	WHITAKER ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *3 and 14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 4-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 September 2001* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

1. Applicant's election of Group I, claims 1-14 and species of chemiluminescent label (claims 2 and 4) in Paper No. 10 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The examiner agrees to rejoin method claim 15, which is dependent on product claim 1, when claim 1 is allowable. Claims 1-14 will be examined.

Sequence Rules Compliance

2. The original filed sequencing listing has complied with Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Information Disclosure Statement

3. The examiner noted that IDS was submitted on November 26, 2001. However, there was no PTO-1449 in the application. Applicant is required to submit PTO-1449 in response to this office action.

4. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper.". Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1, 2, and 4-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 1 is rejected as vague and indefinite in view of item (c) of the claim because it is unclear what mean "one opposite ends of the loop sequence". Since the loop sequence locates at middle region of the nucleic acid probe (hairpin probe) and does not in 5' or 3' of the probe, it is unclear what are opposite ends of the loop sequence. Please clarify.

8. Claim 1 is rejected as vague and indefinite in view of the phrase "wherein said stem structure contains a restriction enzyme cleavage site that is not present in the loop sequence (b) when hybridized to the target nucleic acid sequence" in item (c) of the claim because it is unclear what it intended. Does this phrase mean that said stem structure contains a restriction enzyme cleavage site that is not present in double stranded region formed by loop sequence (b) and a portion of the target nucleic acid sequence when the nucleic acid probe hybridizes to the target nucleic acid or this phrase mean something else? Please clarify.

9. Claim 1 is rejected as vague and indefinite in view of item (d) of the claim because it is unclear what mean "a label located on the opposite side of the restriction site from the surface-coupling group". Since a restriction site is a double region comprising 4-8 bp long in a nucleic acid, it is unclear what means "the opposite side of the restriction site". Does this phrase mean "a

label located on the opposite side of the surface-coupling group or this phrase mean something else? Please clarify.

10. Claim 1 is rejected as vague and indefinite in view of the phrase "wherein said loop sequence makes up all, or part, of the nucleotides between the complementary sequence" in item (d) of the claim because it is unclear what it intended. Does this phrase mean that said loop sequence is fully or partially complementary to the target nucleic acid sequence or this phrase mean something else? Please clarify.

11. Claim 8 is rejected as vague and indefinite because it is unclear what kind of label on the nucleic acid probe. Is the label biotin? Please clarify.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was

made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1, 2, 5-7, 9, 12, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dattagupta (US Patent No. 6,380,377, filed on July 14, 2000) in view of Dahlberg *et al.*, (US Patent No. 5,837,450, published on November 17, 1998).

Note that this rejection was made in view of the ambiguity of claim 5 since claim 1 was rejected under 35 USC 112 (see above).

Regarding claims 1, 7, 12, and 13, Dattagupta taught a hairpin nucleic acid probe comprising a stem region and a loop region wherein the stem region had a restriction enzyme cleavage site and the loop region could form a duplex with the target nucleic acid under suitable conditions (see Figure 1 and columns 3 and 4). Although Dattagupta did not directly show that hybridization of a fully complementary target nucleic acid to the loop sequence of the hairpin probe broke the intramolecular hybridization bonds of the stem structure and removed the restriction site as recited in claim 1, this limitation was considered to be an capability of the hairpin probe since at least one potential target nucleic acid could hybridize with the loop sequence of the hairpin probe and break the intramolecular hybridization bonds of the stem structure and removes the restriction site. The hairpin was covalently attached to a solid support such as a glass as recited in claim 13 by a reactive group (a surface-coupling group as recited in claims 7 and 12) associated with the hairpin probe (see columns 12 and 13).

Regarding claims 5 and 6, in example 2, a 48-mer hairpin probe had a Nla III site (4 bp in length) (see column 23) (for NIA III site, see attached 96/97New England Biolabs Catalog, page 42).

Regrading claim 9, one end of the hairpin probe had a spacer groups (see column 12).

Dattagupta does not disclose a hairpin probe with a label on one end of the probe as recited in claims 1 and 2.

Dahlberg *et al.*, taught that 3' of hairpin probe was attached to a solid support, such as an agarose, styrene or magnetic bead while 5' of hairpin probe had a label such as radioactive, fluorescent, and biotinylated label. If the hairpin structure was not cleaved, the 5' label remained attached to the solid support. If cleavage occurred, the 5' label was released from the solid support as recited in claims 1 and 2 (see column 17). Therefore, it would be obvious to one having ordinary skill in the art at the time the invention was made to know that cleavage of the stem sequences of the probe comprising a restriction enzyme site with the restriction enzyme would detach the label from the surface of the solid support as recited in claim 1.

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have made a hairpin probe with a label on its 5' end as recited in claim 1 in view of the patents of Dattagupta and Dahlberg *et al.*. One having ordinary skill in the art would have been motivated to modify Dattagupta's hairpin probe because the incorporation of a detectable label into a hairpin nucleic acid would enhance direct detection of a hybridization assay, and the simple replacement of one hairpin probe (i.e. a unlabeled probe) from another hairpin probe (ie., a labeled probe) for

constructing an immobilized hairpin probe as recited in claims 12 and 13 would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

14. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dattagupta (July 14, 2000) in view of Dahlberg *et al.,* (1998). as applied to claims 1, 2, 5-7, 9, 12, and 13 above, and further in view of Kacian *et al.*, (US Patent No. 5,935,833, published on August 10, 1999).

The teachings of Dattagupta and Dahlberg *et al.,* have been summarized previously, *supra.* Dahlberg *et al.*, taught that 5' of hairpin probe had a label such as radioactive, fluorescent, and biotinylated label (see column 17).

Both Dattagupta and Dahlberg *et al.,* do not disclose a hairpin probe having an acridinium label as recited in claim 4.

Kacian *et al.*, do teach a DNA probe having an acridinium label (see example 6 in column 16).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have made a hairpin probe having an acridinium label as recited in claim 4 in view of the patents of Dattagupta, Dahlberg *et al.,* and Kacian *et al.*. One having ordinary skill in the art would have been motivated to modify a hairpin probe recited in claim 1 because Dahlberg *et al.,* suggested that the label on a nucleic acid was exchangeable (see third paragraph in column 17) and the simple replacement of one kind of label (ie., a radioactive or fluorescent or biotinylated label) from another kind of label (ie, an acridinium label) during the process of constructing a hairpin probe as recited in claim 4 would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

15. Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dattagupta (July 14, 2000) in view of Dahlberg *et al.,* (1998). as applied to claims 1, 2, 5-7, 9, 12, and 13 above, and further in view of Johnson *et al.,* (US Patent No. 6,372,813, filed on June 25, 1999).

The teachings of Dattagupta and Dahlberg *et al.,* have been summarized previously, *supra.* Dattagupta taught that one end of the hairpin probe had a spacer groups. Amines, hydroxyl, thiol, and carboxyl groups were suitable for attaching the extended portion of the spacer to the surface attaching portion (see column 12).

Both Dattagupta and Dahlberg *et al.,* do not disclose to use polythymine spacers as recited in claim 10.

Johnson *et al.,* teach nucleic acids comprising a spacer region. Polythymine was one kind of spacer (see column 6).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have made a hairpin probe comprising polythymine spacers as recited in claim 10 in view of the patents of Dattagupta, Dahlberg *et al.,* and Johnson *et al.*. One having ordinary skill in the art would have been motivated to modify a hairpin probe recited in claim 1 because the simple replacement of one kind of spacer from another kind of spacer (ie., polythymine spacers) during the process of constructing a hairpin probe as recited in claim 10 would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

16. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dattagupta (July 14, 2000) in view of Dahlberg *et al.,* (1998). as applied to claims 1, 2, 5-7, 9, 12, and 13 above, and further in view of Beattie (US Patent No. 6,156, 502, priority date: December 19, 1996).

The teachings of Dattagupta and Dahlberg *et al.,* have been summarized previously, *supra.* Dattagupta taught that the hairpin was covalently attached to a solid support such as a glass by a reactive group (a surface-coupling group associated with the hairpin probe (see columns 12 and 13).

Both Dattagupta and Dahlberg *et al.,* do not disclose a hairpin probe having a aminopropanol at its 3' end as recited in claim 11.

Beattie does teach to covalently attach an oligonucleotide having a aminopropanol at its 3' end to a solid support (see third paragraph of column 8 and columns 12 and 13).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have made a hairpin probe as recited in claim 11 in view of the patents of Dattagupta, Dahlberg *et al.,* and Beattie. One having ordinary skill in the art would have been motivated to modify the hairpin probe as recited in claim 1 because chemical synthesis of oligonucleotide probes having a aminopropanol at its 3' end using the standard phosphoramidite method was known in the art at the time the

invention was made (see Beattie, column 12, last paragraph) and the simple replacement of one kind of 3' end covalent surface coupling group from another kind of 3' end covalent surface coupling group(ie., 3' aminopropanol) during the process of constructing a hairpin probe would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

17. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dattagupta (July 14, 2000) in view of Dahlberg *et al.,* (1998). as applied to claims 1, 2, 5-7, 9, 12, and 13 above.

The teachings of Dattagupta and Dahlberg *et al.,* have been summarized previously, *supra.* Dattagupta taught that the hairpin probe having 8 bp loop sequences (see column 23).

Both Dattagupta and Dahlberg *et al.,* do not disclose a hairpin probe having 16-25 bp loop sequences as recited in claim 14.

However, in the absence of unexpected results, it would have been obvious to one having ordinary skill in the art at the time the invention was made to have a hairpin probe having 16-25

bp loop sequences as recited in claim 14 in view of patents of Dattagupta and Dahlberg *et al.*. One having ordinary skill in the art has been motivated to modify the hairpin probe recited in claim 1 because optimization of nucleotide number of loop sequence in a hairpin probe would have been obvious to one having ordinary skill in the art at the time the invention was made. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to optimize nucleotide number of loop sequence during the process of constructing a hairpin probe . Note that where the general conditions of a claim are disclosed in the prior art, it is not inventive, in the absence of an unexpected result, to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Conclusion

18. No claim is allowed.

19. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the patent Analyst of the Art Unit, Ms. Chantae Dessau, whose telephone number is (703) 605-1237.

Frank Lu
November 22, 2002

Ethan Whisenant
Primary Examiner